Two Japanese sporadic Creutzfeldt-Jakob disease (sCJD) patients with valine homozygosity at codon 129 of the prion protein gene and PrPSc type 2 (VV2) are described. In contrast with Western countries, this type of sCJD is very rare in Japan. In 123 sCJD cases, only two were recognised as VV2 by the Japanese CJD surveillance committee. The clinical symptoms and pathological findings of the patients were similar to those of European and US patients. The noteworthy finding of diffusion weighted MRI (DWI) was that an abnormal high intensity covered a wide range of the thalamus including the dorsomedial nucleus, the pulvinar, and the ventral anterior, lateral, and posterolateral nuclei. This thalamic pattern has not been recognised in sCJD with methionine homozygosity and PrPSc type 1 (MM1) or methionine/valine heterozygosity and PrPSc type 1 (MV1) which comprises the vast majority of sCJD. This finding may be characteristic to VV2 and may provide a very important clue for the antemortem diagnosis of VV2 subjects.

CASE REPORT
Patient 1 was a 75 year old woman without a family history of prion disease or personal history of neurological disease. She had never received cadaveric growth hormone, dura mater, or cornea. She noticed unsteadiness of gait in February 1999. She visited our outpatient clinic in March 1999 because of this progressive unsteadiness. Neurological examination showed only cerebellar ataxia. The cerebellar ataxia progressed and mild cognitive dysfunctions appeared. In May 1999, she was unable to walk because of advanced cerebellar ataxia, and dementia rapidly progressed. In July 1999, slight myoclonic jerks appeared and she became akinetic and mute thereafter. She died of pneumonia on 4 January 2000.

Cerebrospinal fluid analysis was normal except for an increased concentration of neuron specific enolase (NSE) (77 ng/ml) and the presence of 14-3-3 protein (+). Four sequential EEGs showed no PSWCs during her illness. Diffusion weighted MRI showed an abnormal high intensity in the head of the caudate nucleus, putamen, cingulate gyrus, and insular cortex. A wide range of the thalamus was also involved in the lesion (fig 1A). Genetic analysis of codon 129 of PRNP revealed VV and no point mutation was found. Postmortem examination revealed diffuse spongiform changes, gliosis, and neuronal loss in the cortical ribbon except for the calcarine gyrus where these features were limited to the deep layers. These features were also present in the striatum and thalamus, and marked in the cerebellar granular layer with preserved Purkinje cells. PrP deposition occurred in a plaque-like pattern. Western blot analysis revealed type 2 PrPSc.

Patient 2 was a 69 year old man with no family history of prion disease or personal history of neurological disease. He had never received cadaveric growth hormone, dura mater, or cornea. He noticed unsteadiness of gait in June 2000. He could not continue his accounting work from July 2001. Unsteadiness and intellectual deterioration progressed and dysphagia then appeared. He was admitted to our hospital in September 2001. Neurological examination showed mild dementia, frontal release signs, and cerebellar ataxia. He could walk with the aid of a handrail. Soon after admission, he could not remain sitting. Less prominent myoclonic jerks were evoked by extrinsic stimulation from November 2001.

Abbreviations: DWI, diffusion weighted MRI; EEG, electroencephalogram; PRNP, prion protein gene; PrP, prion protein; PSWC, periodic sharp and slow wave complexes; sCJD, sporadic Creutzfeldt-Jakob disease; vCJD, variant Creutzfeldt-Jakob disease

Cerebrospinal fluid analysis was normal except for an increased concentration ofNSE (110 ng/ml) and the presence of 14-3-3 protein (++). Three sequential EEGs showed no PSWCs during his illness. Diffusion weighted MRI showed an abnormal high intensity in the head of the caudate nucleus, the putamen, the cingulate gyrus, and the insular cortex. Like patient 1, a wide range of the thalamus was also affected by the lesion (fig 1B). Genetic analysis of codon 129 of PRNP revealed VV and no point mutation was found. In the postmortem examination, spongiform changes, gliosis, and neuronal loss in the cortical ribbon and the basal ganglia. ‘‘Pulvinar sign’’ and ‘‘Hockey stick sign’’ are famous MRI findings demonstrating thalamic lesions in vCJD,16 and are included in the diagnostic criteria of vCJD.17 In our patients, however, DWI showed hyperintense lesions in the cortical ribbon, basal ganglia, and a wide range of the thalamus. These thalamic lesions involved the dorsomedial nucleus, the pulvinar, the ventral anterior nucleus, the ventral lateral nucleus, and the ventral posterolateral nucleus. This thalamic pattern is apparently different from that of vCJD. Various lesions in CJD are depicted on MRI; however, the thalamic lesion is rare. Only 7.4% of CJD patients demonstrated thalamic lesion and the changes were only mild.11 We reviewed the DWI findings of our 24 CJD patients comprising 17 sporadic (including one MM-thalamic based on Parchi’s classification1) and one MV as unicommons variants, six familial (one substitution of arginine for methionine at codon 232, one substitution of lysine for glutamine at codon 180), and one iatrogenic CJD (a recipient of cadaveric dura mater) in addition to the present two patients. We found basal ganglia lesions in three, cerebral cortical lesions in six, and both lesions in 15 patients, but could not find thalamic lesions. Including the present two patients, two of 26 (7.7%) CJD patients in our series had thalamic lesions on DWI. Schröter et al,11 Finkenstaedt et al,12 and Samman et al13 described thalamic lesions but they were restricted to the dorsomedial nucleus and pulvinar. Bahn et al14 and Collie et al15 also described thalamic lesions in the dorsomedial nucleus and the pulvinar, respectively. The thalamic lesions that we demonstrated in our two patients involved a wider range of the thalamus than those described in previous reports.11–15 Thalamic lesions that involved almost the entire thalamus were in both our patients and may be a characteristic of sCJD with VV2 rather than merely a coincidence, because such thalamic lesions have not been described before and sCJD with VV2 is extremely rare in Japanese.

Diffusion weighted MRI findings are not included among the major diagnostic criteria,16 although DWI is more sensitive than EEG and can detect lesions at an early stage.11 Even in cases of sCJD without the classical triad, we can make a correct diagnosis more easily if we know the specific imaging finding for a specific subtype. In the case of sCJD with VV2, which does not show prominent myoclonic jerks or PSWCs in the EEG, the characteristic thalamic lesions demonstrated in DWI may lead to an exact diagnosis. These characteristic thalamic lesions can also be an important clue to distinguish sCJD with VV2 from vCJD, because the major differential diagnosis of vCJD is sCJD without PSWCs.

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Magnetic resonance imaging characteristics of sporadic CJD

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